

**Virginia Department of Health**  
**Q Fever: Guidance for Healthcare Providers**  
*Key Medical and Public Health Interventions*

Q fever is a zoonotic bacterial disease caused by *Coxiella burnetii*, an obligate intracellular Gram-negative bacterium. The organism can form a spore-like stage that is highly resistant to heat, drying and many commonly-used disinfectants. *C. burnetii* is highly infectious when aerosolized and inhaled; a single organism may cause clinical illness.

In the United States, Q fever is primarily an occupational hazard related to working with animals (e.g., livestock farms, meat processing plants, veterinary clinics, research facilities with pregnant sheep). Infection most commonly occurs through inhalation of the organism in fine-particle aerosols generated from birth products or fluids during parturition. Infection can also occur through inhalation of dust contaminated with infective birth products, milk or excreta (urine and feces). Less common routes include contact with the birth products, tissue, wool, or bedding from infected animals; laboratory exposure through parenteral inoculation or exposure to infectious aerosols or droplets; ingestion of unpasteurized dairy products from infected animals; through contaminated blood or bone marrow transfusion; and possibly tick bites. Airborne particles can travel downwind a half-mile or more, generating sporadic cases without apparent animal contact.

## **1. Clinical Manifestations**

It is estimated that about half of *C. burnetii* infections are asymptomatic. Symptomatic persons may present with acute or chronic illness.

### **A. Acute Q Fever**

**Incubation period:** 14-21 days (range: 10-39 days) following exposure, depending on infectious dose

**Signs and Symptoms:** Variable presentation

A common presentation of acute Q fever is a self-limited febrile influenza-like illness lasting 2-14 days. The fever usually peaks within 2-4 days, and then resolves after 5-14 days. However, fever may last more than 57 days; therefore acute Q fever is one cause of prolonged fever of unknown etiology. In addition to fever, signs and symptoms may include abrupt onset of fatigue, cough, malaise, chills, sweats, myalgias and headache. Nausea, vomiting, chest pain, diarrhea, sore throat and rash have been less frequently reported.

Another presentation of acute Q fever is pneumonia. This may appear as atypical pneumonia, rapidly progressive pneumonia (mimicking Legionnaire's disease), or most commonly, pneumonia with fever but no pulmonary symptoms. When present, pulmonary symptoms can include a non-productive cough, hemoptysis or pleuritic chest pain. Signs are often minimal, and may include inspiratory crackles or splenomegaly.

Less common presentations of acute Q fever can include hepatitis (fever, abdominal pain, anorexia, nausea, vomiting, diarrhea and jaundice), myocarditis, pericarditis, meningitis, encephalitis or non-specific skin rash. Q fever in pregnant women mainly causes placentitis; cases may be asymptomatic, but generally present with fever. Q fever in pregnancy can cause spontaneous abortion or premature labor.

**B. Chronic Q fever**

**Incubation period:** Months to years after initial exposure

**Signs and Symptoms:** Variable presentation

Endocarditis is the major clinical presentation of chronic Q fever. Non-specific presentations of chronic Q fever may include a generalized illness characterized by a low-grade fever, often remittent and well tolerated, which may be associated with malaise, weakness, fatigue, weight loss, chills, anorexia or night sweats. Manifestations may include digital clubbing, purpuric rash (extremities and mucosa), splenomegaly, hepatomegaly, chronic renal insufficiency, microscopic hematuria and/or embolic manifestations (stroke). Cases may also present with symptoms of heart failure or cardiac valve dysfunction (dyspnea, acute pulmonary edema, angina, palpitations, heart murmur).

Other manifestations of chronic Q fever include chronic hepatitis, vasculitis, osteomyelitis, osteoarthritis, chronic pulmonary infection (fibrosis) or chronic fatigue syndrome.

## **2. Identification and Isolation of Cases**

Although the distribution of Q fever is worldwide, occurrences are rare in the United States. Approximately 25 human cases are reported to Centers for Disease Control and Prevention (CDC) each year. A total of 4 cases were reported in Virginia from 1987-2003.

Person-to-person transmission is extremely rare, but could occur during autopsy of an infected person or during the delivery of a baby from an infected mother. Healthcare workers should use standard precautions for patients with suspected Q fever, although additional precautions may be indicated during a delivery involving a pregnant woman with Q fever.

Q fever is considered a CDC Category B biological terrorism agent. The organism could be used as a biological weapon because of its widespread availability, ease of aerosol dissemination, high infectivity, environmental stability and the possibility of producing large quantities of infectious material. However, *C. burnetii* would be unlikely to cause the large number of deaths that would potentially be caused by Category A agents. If the patient's history does not indicate a possible source of exposure, bioterrorism may be suspected.

### 3. Laboratory Specimens

Diagnosis of Q fever requires specific testing since clinical manifestations are highly variable and nonspecific. **Diagnosis of acute and chronic Q fever is based mainly upon serologic testing to detect antibodies to *C. burnetii* phase I and phase II antigens.\*** The reference method for serodiagnosis is indirect immunofluorescence. For serologic testing, collect an acute blood sample at presentation and a convalescent sample more than 14 days after the acute sample. Collect blood in red top or serum separator tubes and ship refrigerated.

Laboratory tests in addition to serology are available at the Virginia Division of Consolidated Laboratory Services (DCLS) and CDC. Blood, preferably collected before onset of antibiotic therapy, may be tested for *C. burnetii* by nucleic acid amplification (PCR), antigen detection, or culture to aid diagnosis of acute Q fever. Infected tissue (e.g., heart valve in Q fever endocarditis) may be tested by PCR, immunohistochemistry, or culture. Culture can be performed at CDC after consultation, but is not a sensitive method for diagnosis. DCLS must be consulted before specimen submission to verify appropriate tests, specimen collection, and transport. The DCLS Emergency Services Officer can be reached 24 hours a day, 7 days a week at 804-418-9923.

**If Q fever is suspected, laboratory personnel should be alerted to ensure safe specimen processing and selection of appropriate diagnostic tests.** Routine bacteriologic testing will not detect *C. burnetii*.

*C. burnetii* is highly infectious and presents a significant risk of laboratory infection. Biosafety Level 2 practices and facilities are appropriate for nonpropagative laboratory procedures, including serologic testing and staining of impression slides. However, Biosafety Level 3 procedures are necessary for activities involving culture, necropsy of infected animals, or any manipulation of infected tissues. Because *C. burnetii* can grow in a variety of cell lines, it may inadvertently be cultured if infected specimens are placed into routine viral culture.

Additional guidance for laboratories is available in the publication “*Basic Protocol for Level A (Sentinel) Laboratories for the Presumptive Identification of *Coxiella burnetii**” available at the American Society for Microbiology website at [www.asm.org/Policy/index.asp?bid=6342](http://www.asm.org/Policy/index.asp?bid=6342).

### 4. Diagnosis

CDC case definitions for Q fever are shown in Table 1.

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\* *Coxiella burnetii* exists in two antigenic phases called phase I and phase II. In acute cases of Q fever, the antibody level to phase II is usually higher than that to phase I. In chronic Q fever, the reverse is true. High levels of antibody to phase I in later specimens in combination with constant or falling levels of phase II antibodies and other signs of inflammatory disease suggest chronic Q fever. Antibodies to phase I and II antigens have been known to persist for months or years after initial infection. In addition, IgM levels are helpful in the determination of a recent infection.

**Table 1. Case Definitions for Q Fever\***

	<b>Definitions</b>
Clinical Description	<p><i>Acute infection:</i> A febrile illness usually accompanied by rigors, myalgia, malaise and retrobulbar headache. Severe disease can include acute hepatitis, pneumonia and meningoencephalitis. Clinical laboratory findings may include elevated liver enzyme levels and abnormal chest film findings. Asymptomatic infections may also occur.</p> <p><i>Chronic infection:</i> Potentially fatal endocarditis may evolve months to years after acute infection, particularly in persons with underlying valvular disease. A chronic fatigue-like syndrome has been reported in some Q fever patients.</p>
Laboratory Criteria for Diagnosis	<p>a) Fourfold or greater change in Immunoglobulin G (IgG) or Immunoglobulin M (IgM) antibody titer reactive with <i>C. burnetii</i> phase II or phase I antigen in paired serum specimens ideally taken 3-6 weeks apart, or,</p> <p>b) Isolation of <i>C. burnetii</i> from a clinical specimen by culture, or</p> <p>c) Demonstration of <i>C. burnetii</i> in a clinical specimen by detection of antigen or nucleic acid.</p>
Probable Case	A clinically compatible or epidemiologically linked case with a single supportive IgG or IgM titer. The CDC tests for IgG antibodies with an indirect immunofluorescence assay (IFA) and uses a titer of 1:128 as the cutoff for significant antibody. Acute specimens that do not reach this threshold may not rule out clinical illness due to <i>C. burnetii</i> and subsequent testing of convalescent serum would be advised.
Confirmed Case	A clinically compatible or epidemiologically linked case that is laboratory confirmed.

\* Case definitions from the CDC Division of Public Health Surveillance and Informatics. [www.cdc.gov/epo/dphsi/casedef/q\\_fever\\_current.htm](http://www.cdc.gov/epo/dphsi/casedef/q_fever_current.htm). Accessed: March 18, 2005.

## **5. Treatment and Prophylaxis**

### **Treatment of Cases**

Antibiotic treatment is most effective when initiated within the first three days of illness. Therefore, physicians should treat patients based on clinical suspicion rather than awaiting laboratory confirmation which may take several weeks.

A wide variety of recommendations (medications, dosages, and duration) exist for treatment of Q fever. Individual treatment decisions should be made in consultation with an infectious disease specialist. It is very important for patients to complete the entire course of medication; otherwise, patients can experience a relapse that may be harder to treat. Some recommendations that have been proposed in the medical literature for the treatment of acute Q fever and Q fever endocarditis are presented in the Table 2; however, individual treatment decisions should be made in consultation with an infectious disease specialist.

**Table 2. Selected Treatment Regimens for Q Fever**

<b>Acute Q Fever</b>	
Population	Regimen
Adults	<b>Doxycycline</b> , 100 mg PO/IV every 12 hours for 15-21 days OR <b>Tetracycline</b> , 500 mg PO every 6 hours for 15-21 days
Pregnant	<b>TMP/SMX</b> , 160 mg TMP/800 mg SMX PO every 12 hours for duration of pregnancy*
Children <sup>^</sup>	<p>≥ 8 years: <b>Doxycycline</b><sup>+</sup>, 2.2 mg/kg (max: 100 mg) PO/IV every 12 hours for 15-21 days</p> <p>3 months to 7 years: <b>TMP/SMX</b>, 4 mg/kg TMP/20 mg/kg SMX (max: 160 mg TMP/800 mg SMX) PO/IV every 12 hours for 15-21 days</p> <p>Newborns to 2 months: <b>Ciprofloxacin</b><sup>‡</sup>, 10-20 mg/kg (max: 500 mg) PO every 12 hours for 15-21 days</p>
Pre-Existing Valvulopathies or Endovascular Lesions	Doxycycline and Hydroxychloroquine, for 1-12 months Serologic monitoring for 2 years or more
Alternative regimens exist (e.g., chloramphenicol <sup>‡‡</sup> , fluoroquinolones, macrolides, rifampin)	
<b>Q Fever Endocarditis</b>	
<b>Doxycycline</b> , 100 mg every 12 hours and <b>Hydroxychloroquine</b> , 300-600 mg/day for at least 18 months Doxycycline in combination with rifampin or a quinolone may also be used (less effective) Serologic monitoring for reduction in phase I IgG; cardiac valve replacement as indicated	

*Consult an infectious disease specialist for treatment decisions.*

Treatment regimens shown are not necessarily approved by the FDA.

\*TMP/SMX may cause kernicterus at term - consider switching to Ciprofloxacin<sup>‡</sup>, 500 mg PO every 12 hours near term. May require bactericidal combination (e.g., Doxycycline plus Hydroxychloroquine) after delivery.

<sup>^</sup>When benefits of treatment outweigh potential risk from adverse drug reactions.

<sup>+</sup>Doxycycline may cause tooth discoloration in children < 8 years of age.

<sup>‡</sup>Fluoroquinolones may cause cartilage damage in immature animals; none are FDA-approved for use in children less than 18 years of age or in pregnant or nursing women

<sup>‡‡</sup>Higher concentrations (e.g., >25 ug/ml) are associated with increased risk of reversible bone marrow suppression. In addition, chloramphenicol can rarely cause irreversible bone marrow suppression. Children younger than 2 years of age should not receive chloramphenicol.

Adapted from: New York City Department of Health. *Medical Treatment and Response to Suspected Q Fever: Information for Health Care Providers During Biologic Emergencies*. July 2000 Draft. [www.nyc.gov/html/doh/html/cd/qfmd.html](http://www.nyc.gov/html/doh/html/cd/qfmd.html). Accessed: March 9, 2005.

## Post-Exposure Prophylaxis

At the present time, prophylactic antibiotics following potential exposures are not recommended by the CDC since the available evidence does not demonstrate a clear benefit. Routine serologic screening to monitor high-risk persons (e.g., immunosuppression, pregnancy, valvulopathies) after exposure may be appropriate.

However, antibiotic prophylaxis may be considered for some high-risk persons. If implemented, chemoprophylaxis should begin **no earlier than 8-12 days AFTER exposure**. If given too early after exposure (0 to 7 days), then chemoprophylaxis may not be effective and may simply prolong the incubation period.

Non-pregnant adult regimens for chemoprophylaxis that have been proposed include doxycycline 100 mg PO every 12 hours or tetracycline 500 mg PO every 6 hours for 5-7 days. For pregnant women, 160 mg of trimethoprim (TMP) in combination with 800 mg of sulfamethoxazole (SMX) PO every 12 hours for the duration of pregnancy, is the preferred antibiotic. However, at term, when the risk of kernicterus is greatest, consider switching to a fluoroquinolone, such as ciprofloxacin (500 mg PO every 12 hours). (Source: New York City Department of Health)

Pediatric regimens for chemoprophylaxis that have been proposed include doxycycline 2.2 mg/kg (max: 100 mg) PO every 12 hours for children  $\geq 8$  years of age; trimethoprim 4 mg/kg plus sulfamethoxazole 20 mg/kg PO every 12 hours for 5 days for children  $> 2$  months but  $< 8$  years of age; or ciprofloxacin 10-20 mg/kg PO (max: 1 g/day) every 12 hours for 5 days for newborns to 2 months of age. (Source: New York City Department of Health)

## **6. Vaccine**

In the United States, Q fever vaccine is not commercially available for general use. The U.S. Army has an investigational vaccine.

## **7. Decontamination**

*C. burnetii* may survive for months or years in its spore form, and can resist heat, desiccation, and many commonly used disinfectants (e.g., bleach, Lysol). Therefore, special decontamination procedures are necessary for surfaces potentially contaminated with *C. burnetii*. Minor spills should be covered with absorbent paper, such as paper towels, and then flooded with 70% ethanol or 5% MicroChem-Plus (a dual quaternary ammonium compound), which should be allowed to act for 30 minutes before cleanup. Spills that involve high concentrations of organisms, include organic matter, or occur in areas of lower temperatures (e.g., refrigerators or freezers), should be exposed to disinfectant solution for 1 hour before cleanup.

Hospital rooms of patients with Q fever should receive terminal cleaning consistent with the above precautions, and clothing or linens should be disinfected according to hospital protocol.

## **8. Postmortem Practices**

If Q fever is suspected as a cause of death, the regional Office of the Chief Medical Examiner (OCME) should be immediately notified. Consultation should occur regarding whether an autopsy should be conducted, the parties responsible for conducting the autopsy, and the appropriate personal protective procedures to follow.

## 9. Public Health Measures

- A. Suspected cases should be reported to hospital epidemiology/infection control, who in turn should notify laboratory personnel, other medical care providers and the local health department.
- B. Laboratory specimens should be sent to DCLS for confirmation of the agent and other studies.
- C. The designated public health authority should begin an epidemiologic investigation.
  - a. Collect detailed information from the patient about animal exposures and other possible sources (e.g., consumption of unpasteurized dairy products).
  - b. Investigate contacts of the case for compatible illness that may be due to a common exposure.
  - c. Suspected food items (e.g., unpasteurized milk or cheeses, etc.) should be collected for possible testing. The Virginia Department of Health (VDH) Office of Epidemiology will work with the Food and Drug Administration (FDA) if commercially prepared food is implicated.
  - d. If animal exposures are identified, the Virginia Department of Agriculture and Consumer Services (VDACS) will be notified.
  - e. If an intentional release (i.e., bioterrorism) is suspected, law enforcement personnel will be notified.

### References

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